



Facing Hereditary Cancer EMPOWERED

April 3, 2024

Senator Bill Cassidy

Ranking Member, Senate Health, Education, Labor, and Pensions (HELP) Committee

455 Dirksen Senate Office Building

Washington, DC 20510

Submitted to diagnostics@help.senate.gov

Re: RFI on Clinical Diagnostics

Senator Cassidy and esteemed members of the Senate HELP Committee,

We appreciate the opportunity to provide input regarding oversight of clinical diagnostic tests, known as in vitro diagnostics (IVDs) and laboratory-developed tests (LDTs). FORCE (Facing Our Risk of Cancer Empowered) is a national nonprofit organization representing the millions of Americans with or at increased risk of hereditary cancers due to an inherited genetic mutation such as BRCA1, BRCA2, ATM, CHEK2, PALB2, Lynch syndrome, etc. Our community relies heavily on LDTs and IVDs to identify those with a hereditary predisposition to cancer and guide treatment of those diagnosed with the disease.

While access to “timely and advanced diagnostics” is important, vigilant oversight of these tests is crucial to mitigate potential harm incurred by inaccurate or unsafe tests. Accordingly, we have actively engaged with Congress and the FDA regarding proposals to reform diagnostics regulation. Please see the below responses to the questions posed in the request for stakeholder information. We have provided perspective on the topics where our organization has knowledge/expertise.

FDA Regulatory Framework for Diagnostics

1. *How well is FDA’s medical device framework working for the regulation of diagnostic products? Are there improvements that should be made?*
 - a. *Of these specific changes, which would require Congressional action, and which can be effectuated by FDA alone?*

We believe the current framework for regulation of diagnostic products generally works well. It can be adapted and expanded, as proposed by the FDA, to include oversight of all IVDs and LDTs. Congressional involvement should be minimal.

2. *Does the current device regulatory framework support the review of diagnostics that are developed using AI or that incorporate AI?*

We urge caution in the use of AI in the development and review of diagnostics given the new and relatively untested nature of this technology. We do not believe that AI can supplant human evaluation at this point. While efficiency in technology development and obtaining patient test

results is beneficial, we prioritize patient safety and reduction of harm. At this time, it is unclear how to evaluate AI technology use in healthcare and therefore we suggest that this approach be limited until evidence-based data is developed to determine its utility and the processes for adequate evaluation of quality and risks.

3. *What, if anything, makes diagnostics distinct among FDA-regulated medical products to warrant specific attention to how AI may be used in the review of product submissions?*

As stated in our response to Question 2, we urge caution in the use of AI in the development and review of diagnostics given the new and relatively untested nature of this technology. Currently, we do not believe that AI can supplant human evaluation of medical products. We suggest limited use of AI until evidence-based data is developed to ascertain its utility and the processes for quality- and risk-evaluation.

4. *Are the regulatory pathways intended to evaluate diagnostics for special populations (i.e. rare diseases or genetic disorders) working?*
 - a. *How could they be enhanced to accelerate and authorize products for special populations, for example, certain companion diagnostics for rare biomarkers?*

We believe the current system works relatively well. Expediting authorization of medical devices and products also increases potential risk. Patients make potentially life-altering, irreversible decisions based on genetic test results. For example, based on medical guidelines, a woman with a BRCA genetic mutation may undergo a risk-reducing hysterectomy or mastectomy. An error can have catastrophic implications. As such, test accuracy is critical.

5. *Are there regulatory hurdles to expanding the settings in which diagnostics are performed, i.e. point-of-care (POC) tests performed in patients' homes?*
 - a. *In what ways could/should FDA leverage regulatory flexibilities to reduce testing barriers?*

The FDA has already allowed flexibility in germline testing for hereditary cancer mutations. Over-the-counter, direct-to-consumer tests such as 23andMe have facilitated broader access with the caveat that these tests are not comprehensive and serve more recreational purposes. As such, they have resulted in a great deal of confusion among consumers because there is no engagement with qualified healthcare providers.

A confirmatory, medical-grade test is advised if a mutation is identified to ensure the accuracy of test results via more stringent quality control. Additionally, direct-to-consumer test results are not accepted by health insurers so medical-grade testing must be done to facilitate appropriate care and risk management.

For medical-grade hereditary cancer genetic tests, patients can pursue testing directly through a lab. A test kit to collect a saliva sample can be ordered online and sent to the consumer's home. This makes testing very accessible. In addition, the labs provide access to virtual genetic counseling, a crucial component of genetic testing.

We do not recommend the expansion of consumer-grade, home-based diagnostic testing at this time. The risk of patient error and misunderstanding is too great, and many tests will need to be confirmed via additional medical-grade testing.

6. *What are your views on FDA's implementation of predetermined change control plans; is FDA's approach in its recent guidance readily applicable to IVDs and other diagnostic products?*

Genetics is a complex, rapidly growing field that affects virtually every area of medicine. Accurate, high-quality tests and oversight of marketing practices are critical as more consumers base medical decisions such as increased cancer screening or risk-reducing surgeries on genetic test results. We cautiously support the FDA's recently announced ruling regarding Medical Devices; Laboratory Developed Tests (Docket No. FDA-2023-N-2177).

The proposed FDA rule on Medical Devices; Laboratory Developed Tests can be effective for oversight of IVDs and other diagnostic products with some adaptations. We see the need for FDA oversight to reduce potential harm incurred by inaccurate or unsafe tests as well as false or fraudulent marketing practices (which we've seen in the genetic testing space in recent years). At the same time, we recognize that FDA enforcement of authority over LDTs as medical devices may increase patient costs and reduce access (particularly to small laboratories), and could affect innovation if labs and manufacturers choose not to invest or seek FDA approval or clearance due to the perceived time and financial costs.

7. *Does FDA's current risk classification framework properly measure risk versus regulatory controls for diagnostics products?*

a. *If not, how can FDA's risk-based regulatory approach to diagnostics be improved to better align the degree of regulatory oversight with patient risk and benefit?*

We believe the 3-class system—Class I for low-risk tests, Class II for moderate-risk tests, and Class III for high-risk tests—is appropriate for IVDs/LDTs. This framework adequately reflects test impact on patients, but we have questions and concerns about the FDA's proposed down-classification of tests. We encourage the agency to clearly define which tests fit into each category and to ensure:

- Patient protection from poorly performing tests
- Safety and efficacy of targeted therapies
- A level playing field for tests with similar intended uses
- Equal access to single gene and multigene genetic tests

8. *In considering reforms to FDA's risk classification framework for diagnostics, what types of IVDs should be exempt from premarket review?*

a. *What factors related to risk management should be applied to risk classification of IVDs?*

Low-risk tests should continue to be exempt from premarket review. We believe moderate- and high-risk IVDs/LDTs should undergo pre-market review. In addition, currently available moderate- or high-risk tests should not be grandfathered in perpetuity; just because a test is currently on the market doesn't mean it is a good, clinically and analytically accurate IVD/LDT.

9. *Is the “safety and effectiveness” standard against which diagnostics are reviewed the most appropriate review standard to assign risk management for clinical tests?*

Yes, we support the 3-class system for safety and effectiveness—Class I for low-risk tests, Class II for moderate-risk tests, and Class III for high-risk tests—and maintain that this framework is needed to protect patients from potential harm.

10. *Do the proposed reforms to FDA’s device framework warrant the establishment of a new regulatory pathway specific to diagnostics? If yes, what are the principles that should guide such a new framework, as it would be applied to diagnostics currently subject to FDA premarket review?*

Creating a new framework will likely lead to loopholes and lack of harmonization between processes that would add burden, cost, and create confusion. Evaluation of diagnostics/IVDs/LDTs is best done using the current framework with adaptations as needed.

CLIA Regulatory Framework for LDTs

1. *What updates to the clinical laboratory regulatory structure under CLIA should Congress consider to reflect the latest scientific practices and safety standards?*

No comment.

2. *What are your views on the effectiveness and use of the Clinical Laboratory Improvement Advisory Committee (CLIAC) in providing scientific and technical guidance to inform potential updates to CLIA standards?*

No comment.

3. *Do the proficiency testing programs currently approved by the Department of Health and Human Services (HHS) reflect the latest clinical standards of laboratory medicine? Are there specialties, subspecialties, or analytes that should receive greater consideration for HHS approval?*

No comment.

4. *How well does the existing enforcement structure under CLIA work in ensuring compliance with regulatory requirements and taking action against noncompliance? What should be improved, if anything at all?*

It would be helpful to move the existing CLIA process under the umbrella of the FDA to allow enforcement coordination as well as reporting of CLIA evaluations to maintain and update test approval status. CLIA and the FDA should work collaboratively.

5. *Should legislative reforms address CLIA’s quality system requirements? If yes, which of those changes would require Congressional action, and which could be effectuated by CMS alone?*

No, even with input from the community, we do not believe that Congress has the expertise to adequately address CLIA quality system requirements. These vary by industry and should remain under the auspices of CMS or the FDA rather than be specified by Congress.

6. *Where does redundancy exist, if at all, within the current CLIA regulatory structure with respect to accreditation standards under federal and state licensure programs, as well as through CMS-approved accreditation organizations?*

No comment.

7. *In considering legislative reforms to CLIA, should LDTs be defined in statute? What aspects of test development would characterize such a definition?*

LDTs and IVDs are medical products/tests. If Congress must be involved, it should collaborate with the FDA to develop definitions for these devices.

8. *How should Congress consider issues relating to the practice of medicine and its relationship with labeling for LDTs? Should there be additional oversight of the information conveyed to patients serviced by LDTs?*

With sufficient funding, agencies such as the FDA, CDC, HHS and CMS are qualified and well-equipped to communicate information about LDTs. The practice of medicine is best left to the licensed healthcare providers rather than be legislated. Medical treatment needs to be adaptable in response to timely, real-world patient needs that vary widely.

9. *Should certain CLIA regulations be updated, would it necessitate a reevaluation of the CLIA fee schedule?*

If the FDA and CLIA work together, it may not be necessary to reevaluate or adjust the CLIA fee schedule. As a patient advocacy organization, we recognize that increased diagnostic and healthcare costs are often passed on to patients. We urge that costs are not unnecessarily increased as this would likely exacerbate patient access barriers. We support a process that balances costs and test accuracy, validity, reliability, patient safety and access.

10. *What compliance challenges would legislative reforms to CLIA create? How should new regulatory requirements apply to tests currently available to patients?*

It has been proposed that tests currently on the market should be grandfathered. We oppose this. Regulatory requirements should apply to all new tests as well as those currently available to ensure high-quality, reliable diagnostics. That said, we acknowledge that moving to a new regulatory framework may entail considerable effort for both those offering diagnostic testing and the regulatory authorities evaluating them. We suggest a process that provides a defined phase in period (e.g. 5 years) of the new regulatory requirements for existing LDTs/IVDs, while requiring new tests to be evaluated before being made available to the public.

Need for Post-Market Authority

One reason we see the need for FDA involvement and oversight of LDTs/IVDs is its ability to enforce post-market authority to preserve patient safety. Regulators need continuous insight into the performance of tests once they have reached the market, and the ability to request information from developers about the validity and quality of their tests. When a test appears to be delivering inaccurate

and/or unreliable information to patients and providers, it is imperative that the oversight agency act, i.e., instituting additional safeguards to mitigate risks or requiring that the test be taken off the market.

With the expansion of genetic testing, we have seen an increase in fraudulent practices—often targeting our most vulnerable citizens. In many cases, individuals with little or no healthcare background or genetics training have marketed and facilitated genetic testing for a hereditary predisposition to cancer (e.g., BRCA and similar genetic mutations) at community health fairs, senior centers, nursing homes, etc.

Often, consumers were misadvised regarding their eligibility for insurance coverage (e.g., Medicare) of their testing. In some cases, those tested never received test results. In other cases, the results were delivered by individuals who should not be engaged in the collection, interpretation or communication of medical information. As noted above in the comments regarding risk categories, inappropriate genetic testing or misinterpretation of results can lead to serious adverse outcomes for patients and their families.

In 2019, our organization filed complaints against several labs and companies for false claims and unscrupulous behavior with the OIG, FTC, and state attorneys general. It is important to note that these tests are overseen by CLIA, which has no authority over marketing practices. At the time, the FDA did not exercise regulatory oversight of LDTs unless they were FDA-cleared or -authorized. We are hopeful that the proposed rulemaking and subsequent engagement of the FDA will provide consumer protections and a clear pathway for future issues of this nature.

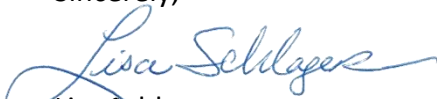
In Closing

LDTs/IVDs are essential to the timely diagnosis and treatment of numerous diseases and conditions. As such, it is crucial to ensure that these tests are safe and accurate while maintaining patient access and minimizing the costs of care. With the growing complexity and number of these tests, additional review and oversight are greatly needed.

At the same time, the proposed changes (via the FDA, VALID Act, etc.) would significantly modify regulatory oversight, compelling many laboratories to comply with premarket review, quality systems, labeling, medical device reporting and other requirements. These processes are unfamiliar to most laboratories so significant guidance and the phased rollout of any changes will be crucial in effectively facilitating this process with minimal disruption to healthcare providers and the patients they serve.

Thank you for your consideration of our feedback. We look forward to a continued dialogue and welcome future opportunities to the needs and perspectives of our community.

Sincerely,



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